HIV update : 2020

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- The activity planners and speaker do not have any financial relationships with commercial entities to disclose.

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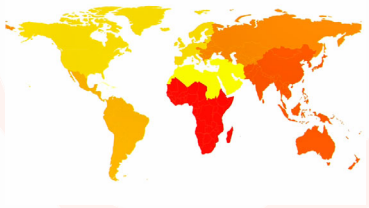
Objectives

- Discuss COVID-19 in people with HIV (PWH)
- Recognize currently recommended therapies for PWH
- Report new HIV therapy options
- Identify current HIV prevention plan



- 1.7 million new infections in 2018 worldwide
- 4700 new infections a day

UNAIDS GAP report 2019

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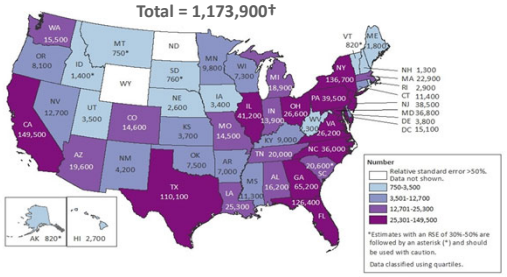
Estimated HIV Prevalence among Persons Aged ≥13 years, by Area of Residence 2018—United States

Total = 1,173,900†



CDC

Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Estimates rounded to the nearest 100 for estimates >1,000 and to the nearest 10 for estimates ≤1,000 to reflect model uncertainty. Estimates for the year 2018 are preliminary and based on deaths reported to CDC through December 2019. Estimates for Alabama, Oklahoma, and South Carolina should be interpreted with caution due to incomplete death ascertainment.
†Total estimate for the United States does not include data for Puerto Rico.

COVID 19 epidemic

Global Confirmed
56,051,621

Global Deaths
1,345,851

U.S. Confirmed
11,468,739

U.S. Deaths
249,935

Global Map ›

DATA IN MOTION
COVID-19 Data in Motion: Wednesday, November 18, 2020
A 60-second, daily summary of the most important data on COVID-19 in the U.S., updated every morning.

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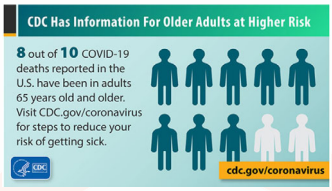
John Hopkins Coronavirus Resources

Risk Factors for Severe COVID-19

- Cancer
- Heart disease
- COPD
- Chronic kidney disease
- Immunocompromise from solid organ transplant
- Obesity
- Sickle cell disease
- Smoking
- Type 2 diabetes

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html



https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/older-adults.html

Is HIV a Risk Factor for COVID-19?

- ISARIC WHO Clinical Characterization Protocol (UK): COVID-19 Hospitalizations in PLWH

At Hospitalization for COVID-19

	With HIV (n=122)	Without HIV (n=47,470)
Age (years)	56*	74
Male (%)	66	57
White/black/other (%)	46*/43*/11	84/4/12
Number of comorbidities (median)	1*	2
Systemic symptoms (%)	89*	69
Presenting symptoms (%)		
Fever	83*	65
Myalgia	27†	18
Headache	19†	11
Cough	79†	66
Dyspnea	73	68
Chest pain	23†	14
Sore throat	14†	8

*P<0.001 and †P<0.05 versus without HIV.

- Prospective, observational study of people with COVID-19 infection (January-June 2020; n=47,592,207 from 207 centers)
  - HIV coinfection (0.26%; 90% on ART) 123 people
- Outcome: association between HIV status and mortality at day 28
- Characteristics of persons with HIV (versus no HIV) at time of hospitalization for COVID-19
  - Younger
  - Fewer comorbidities
  - More systemic symptoms
  - Higher lymphocyte counts and C-reactive protein levels
- Geretti AM, et al. *Clin Infect Dis.* 2020;Oct 23

ISARIC WHO Clinical Characterization Protocol (UK): COVID-19 Hospitalizations in PLWH

- Cumulative day-28 mortality was similar among persons with and without HIV (27% versus 32%)
- Mortality was higher among people with HIV after adjusting for
  - In an adjusted analysis mortality was higher among people with HIV (adjusted hazard ratio 1:52 to 1:92)
- Within the HIV positive group
  - Those who died by day 28 (versus survived) were older and had a higher prevalence of diabetes and obesity and were less likely to have a record of ART
- Geretti AM, et al. *Clin Infect Dis.* 2020;Oct 23

Selected Characteristics of Patients With HIV by Outcome at Day 28

	Died (n=30)	Alive (n=92)
Age (years)	58*	55
ART recorded (%)	81*	95
Comorbidities (%)		
Diabetes, with complications	17†	5
Obesity	29†	13
Laboratory parameters		
WBC (x10⁹/L)	8.0†	5.6
Glucose (mmol/L)	10.4†	6.4
Hyperglycemia (%)	40†	13
C-reactive protein (mg/L)	187*	92

*P<0.01 and †P<0.05 versus alive.

Mount Sinai Hospital System: Laboratory Confirmed COVID-19 and Persons With HIV on ART

- Cohort study (March-April 2020)
  - Persons with HIV hospitalized for laboratory confirmed COVID-19 (n=88)
  - Controls with COVID-19 and without HIV
    - Matched for age, sex, race/ethnicity, and calendar week of infection
- Persons with HIV
  - On ART: 100%
  - HIV RNA <50 copies/mL: 81%
  - Greater proportion of smoking and comorbid illness compared with matched controls

Sigel K, et al. *Clin Infect Dis.* 2020;Jun 28

Cohort Characteristics

	With HIV (n=88)	Without HIV (n=405)
Median age (years)	61	60
Male (%)	75	76
White/black/Hispanic (%)	19/40/28	19/42/28
Comorbidities (%)		
Current former smoker	55*	23
COPD	9*	2
Cirrhosis	6†	2
Cancer	17*	6
Obesity	10	8
Hypertension	38	33
Diabetes mellitus	27	29
Chronic kidney disease	22	14

*P<0.001 and †P<0.05 versus controls.

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Mount Sinai Hospital System: Laboratory Confirmed COVID-19 and Persons With HIV on ART

- No difference in COVID-19 severity on admission by HIV status (*P*=0.15)
- Poor outcomes for hospitalized persons with HIV were frequent but similar in proportions with matched controls
- Similar cumulative incidence of death over time by HIV status (*P*=0.9)

Sigel K, et al. *Clin Infect Dis.* 2020;Jun 28

COVID-19 Presentation and Adverse Outcomes

	With HIV (n=88)	Without HIV (n=405)
Severity on admission (%)		
Mild	18	22
Moderate	44	32
Moderate/severe	17	24
Severe	21	22
Adverse outcomes (%)		
Mechanical ventilation	18	23
Death	21	20

Severity on admission based on oxygen supplementation requirement:
Mild (no supplemental oxygen).
Moderate (nasal cannula or Venturi mask).
Moderate/severe (non-rebreather mask, high-flow nasal cannula).
Severe (non-invasive ventilation or mechanical ventilation).

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Disproportionate Burden of COVID-19 Among Racial Minorities and Those in Congregate Settings

- Outbreak March 3 - April 26, 2020 in Boston, MA
  - 36 people with HIV with confirmed COVID-19
  - 11 with probable infection
- Social Disparities
  - 77% of those with diagnosed or suspected COVID-19 were non-Hispanic Black or Latinx - only 40% of the clinic population is Black or Latinx
- 85% had non-HIV comorbidity:
  - Obesity, hypertension, cardiovascular disease
- 44% exposed to long-term care settings

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Meyerowitz EA. AIDS 2020, 34:1781–1787

VACS Study: COVID-19 Testing, Positivity, and Outcomes in Persons With and Without HIV

- Open cohort study (through June 2020)
  - Electronic health records database of veterans with HIV and matched controls without HIV
    - Persons with HIV were slightly younger, lower BMI, and more current smokers versus matched controls without HIV
- Outcomes
  - COVID-19 molecular testing, positive tests, and severe disease (hospitalization, intensive care, intubation, death)
- Key results over 113-day study
  - PLWH had a higher proportion of COVID-19 testing
  - No difference between PLWH and matched controls without HIV in susceptibility to COVID-19 or risk of severe disease
- Park LS, et al. *J Int AIDS Soc.* 2020;23(suppl 4). Abstract LBPEC23

COVID-19 Testing

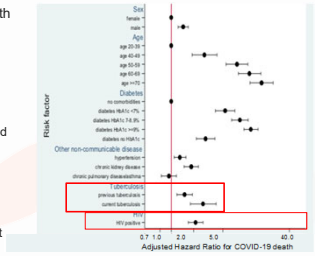
	PLWH (n=30,981)	No HIV (n=76,745)	Adjusted Odds Ratio (95% CI)
Tested for COVID-19 (%)	8	7	1.36 (1.29, 1.43)
COVID-19 positive (%)	10	10	1.05 (0.89, 1.24)

Outcomes Among COVID-19 Positive

	PLWH (n=253)	No HIV (n=504)	Adjusted Hazard Ratio (95% CI)
Hospitalization	34	35	1.09 (0.85, 1.41)
Intensive care admission	14	15	1.08 (0.72, 1.62)
Intubation	6	8	0.89 (0.49, 1.59)
Death	10	11	1.08 (0.66, 1.75)

Risk factors for COVID-19 Death-Western Cape Province, South Africa

- Population cohort study (n=3,460,932, 16% with HIV)
  - Diagnosed with COVID-19: 0.65% (n=22,308)
  - Died: 2.8% (625/22,308)
- HIV was associated with increased risk of COVID-19 mortality
  - Adjusted HR: 2.14 (95% CI 1.70, 2.70)
  - Similar risks across strata of HIV RNA levels and immunosuppression
- Limitations
  - Potential under-ascertainment of comorbidities
  - Lack of data on other potential risk factors (eg, socio-economic status, BMI)
  - Relatively large number of PLWH without recent viral load or CD4 count results



Boulle A. Clin Infect Dis 2020 Aug 29;ciaa1198.

COVID-19 Outcomes Among Registry of Patients With HIV

- Consecutive patients with HIV and laboratory confirmed COVID-19 infection (April-July 2020; n=286)
- Primary endpoint: severe outcome (composite of ICU admission, mechanical ventilation, or death)
  - All patients (18%), among hospitalized patients (31%)
- Overall mortality: 9.4% (27/286)
  - Among those hospitalized: 17% (27/164)
  - Among those admitted to the ICU: 52% (24/47)
- Factors associated with severe outcomes
  - Older age, chronic lung disease, hypertension, lower CD4 count (<200 cells/mm^3), ≥3 comorbidities
  - No association: ART regimen or lack of viral suppression

Factors Associated With Hospitalization and Severe Outcome

	Adjusted Odds Ratio (95% CI)	
	Hospitalization	Severe Outcomes
Age (years)	1.08*(1.04-1.07)	1.04* (1.0-1.07)
CD4 (ref. >500 cells/mm^3)		
200-500	1.12* (1.1-12.22)	1.93 (0.73-5.06)
<200	3.67† (1.64-17.1)	2.8* (1.02-7.67)
Chronic kidney disease	4.08† (1.45-11.52)	--
Chronic lung disease	4.06† (1.87-8.81)	3.37† (1.63-6.97)
Hypertension	--	2.43† (1.2-4.93)
Comorbidity burden (ref. no comorbidities)		
1 or 2	1.13 (0.49-2.6)	2.21 (0.42-11.7)
≥3	3.57† (1.29-9.9)	5.40* (1.02-28.54)

*P<0.05 and †P≤0.01.

Dandachi D, et al. *Clin Infect Dis.* 2020;Sept 9

HIV Viral Suppression Rates During COVID-19: Ward 88, San Francisco

- Single-center cohort study of HIV care pre versus post shelter-in-place (12/19-2/20 versus 4/20-5/20)
- HIV RNA <200 copies/mL pre shelter-in-place (n=1766): 81%
- Post shelter-in-place (versus pre)
  - Odds for patients having HIV RNA ≥200 copies/mL increased 31%
    - Increased odds among blacks (versus white) and homeless
  - Retention-in-care increased slightly
    - Facilitated by an increase in telehealth visits

Adjusted Odds Ratio (95% CI) (post versus pre shelter-in-place)

	HIV RNA ≥200 Copies/mL*	No-Show Visits
Overall	1.31 (1.08-1.53)	0.91 (0.77-1.09)
Female versus male	0.94 (0.77-1.15)	0.99 (0.80-1.21)
Race/ethnicity (ref. white)		
Black	1.60 (1.33-1.91)	1.14 (0.94-1.38)
LatinX	1.04 (0.63-1.34)	1.06 (0.88-1.27)
Asian	0.92 (0.63-1.34)	1.16 (0.82-1.64)
Other	0.96 (0.78-1.19)	0.97 (0.77-1.24)

*Propensity score analysis.

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Spinelli MA, et al. *AIDS*. 2020;Sept 7

Impact of COVID-19 on HIV PrEP Care at a Boston Community Health Center

- Fenway Health center (n=3520; January-April 2020)
  - Baseline characteristics
    - Age (37 years), white/black/Hispanic/other (73%/6%/14%/7%)
    - Cisgender male (92%)
    - Public/private insurance (13%/86%)
- There was a major shift from in-person visits to telehealth (24 versus 1022 visits)
- PrEP refill lapses were associated with age (*P*=0.001), race (*P*=0.001), ethnicity (*P*=0.04), and insurance type (*P*=0.002)
- Limitation: cannot ascertain sexual and pill-taking behaviors
- Results indicate COVID-19 was associated with major disruptions in PrEP refills, new starts, and HIV/STI testing, despite near-complete shift to telehealth

Main Changes in PrEP Care (January to April 2020)

	Change (%)
New PrEP starts	-72
Patients with an active PrEP prescription	-18
Tests	
HIV	-85
Gonorrhea/chlamydia	-85
Positive gonorrhea/chlamydia	-81
Percentage of positive gonorrhea/chlamydia test	+4

- Krakower D, et al. *J Int AIDS Soc*. 2020;23(suppl 4):176-177. Abstract OACLB0104

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Impact of COVID-19 Related Shelter-in-Place Orders on PrEP Access, Usage, and HIV Risk Behaviors

- Electronic convenience sample survey of PrEP users (n=394) and providers (n=188)
- Providers via email (Academy of HIV Medicine database) and users via social media
- Findings from this survey indicate that providers faced challenges adhering to CDC recommended monitoring and testing and that telemedicine was a critical component of PrEP access during Shelter-in-Place Orders

- Brawley S, et al. *J Int AIDS Soc*. 2020;23(suppl 4):178. Abstract OACLB0101

Changes during shelter in place orders

Among PrEP users

- Stopped PrEP use: 32%
  - Main reasons: decreased perception of risk (88%), lack of access (8%)
- No change or increase in risk behaviors: 10% to 15%
  - Suggests ongoing PrEP access is important to mitigate HIV risk

Among PrEP providers

- Prescribed new PrEP prescriptions and refills: 55% (refills only: 41%)
- Reported at least 1 patient stopped PrEP
- Encountered patients with possible self-reported STI, but unable to test: 81%
- Empirically treated patient for STI without seeing them or a test: 53%

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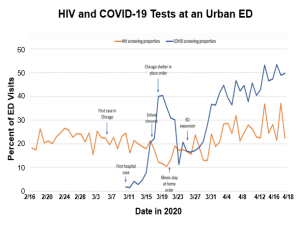
Routine Screening for HIV During the COVID-19 Pandemic

- Urban ED preparations
  - Established a large temporary space for screening, testing, and treatment of patients with influenza-like illness who were considered likely to be discharged home
  - Continued HIV screening of patients was incorporated into the design of this secondary ED space, with a station for lab draws designated for HIV screening
- HIV testing (percent of ED visits) was maintained during first 1.5 months
  - Through 4/18: 6 persons tested positive for HIV
- It is important to maintain HIV screening and linkage to care, even in the face of the COVID-19 pandemic
  - HIV elimination initiatives nationwide require expansion and intensification of HIV screening and linkage to care efforts



- Stanford KA, Friedman EE, Schmitt J, et al *AIDS Behav*. 2020;24:2757-2759.

ART for People with HIV and COVID-19

- To date, there is no clear evidence suggesting a benefit of a particular HIV antiretroviral regimen in people with COVID-19 and HIV
- People should not have their HIV regimen changed or have antiretrovirals added in order to prevent or treat COVID-19

DHHS.gov. Interim Guidance for COVID-19 and Persons with HIV. Available at https://clinicalinfo.hiv.gov/guidelines/covid-19-and-persons-hiv-interim-guidance/interim-guidance-covid-19-and-persons-hiv

DHHS Interim Guidance for COVID-19 and PWH

- Disease course of COVID-19 in persons with HIV does not differ from that in persons without HIV (based on limited data)
  - It is not yet known whether advanced HIV infection (ie, CD4 cell count <200/mm^3) is a risk factor for complications of COVID-19
- Comorbidities (eg, CVD or lung disease) in persons with HIV increase the risk for a more severe course of COVID-19 illness
  - This includes chronic smokers
- Until more is known, additional caution for all persons with HIV, especially those with advanced HIV or poorly controlled HIV, is warranted
- Influenza and pneumococcal vaccinations should be kept up to date
- Persons with HIV should follow all applicable CDC recommendations to prevent COVID-19 (eg, social distancing, proper hand hygiene

- DHHS. June 19, 2020. https://clinicalinfo.hiv.gov/en/guidelines/covid-19-and-persons-hiv-interim-guidance/interim-guidance-covid-19-and-persons-hiv?view=full.

DHHS Interim Guidance for COVID-19 and PWH: Antiretroviral Therapy

- Persons with HIV should
  - Maintain on-hand ≥30-day supply, and ideally a 90-day supply, of medications
  - Consider changing to mail order delivery of medications when possible
  - If a regimen switch is planned, consider delaying the switch until close follow-up and monitoring are possible
- Persons with HIV should not switch their ART regimens or add antiretroviral drugs to their regimens for the purpose of preventing or treating SARS-CoV-2 infection

- Clinic/Laboratory Monitoring Visits Related to HIV Care
- Weigh risks/benefits of attending versus not attending in-person, HIV-related clinic visits
  - Consider extent of local COVID-19 transmission, health needs to be addressed during the appointment, HIV status, and overall health
- Consider telephone/virtual visits for routine or non-urgent care/adherence counseling
- If virally suppressed and in stable health, routine medical and laboratory visits should be postponed to the extent possible

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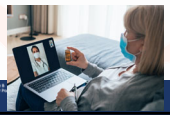
Telehealth

Pros

- Convenient
  - Eliminate costs/difficulties of transportation
  - No need for childcare
  - Less time off work needed
- May enable better medication reconciliation
- Many insurances now reimbursing



Cons

- Concerns re: client confidentiality
- Many providers lack telehealth with equipment to allow patient exam
- May exacerbate social disparities
  - Lacking phone or computer
  - Low health literacy or technology literacy
- Problems with internet connections
- Lack of face to face interactions which can negatively affect patient-provider rapport

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DHHS Interim Guidance for COVID-19 and Persons With HIV: Pregnant Individuals and Children

- **Pregnant Individuals With HIV**
- Limited information on pregnancy/maternal outcomes
- Possible increased susceptibility to viral respiratory infections, including COVID-19
- Adverse pregnancy outcomes were noted in a small series of pregnant women with COVID-19 (also seen with SARS and MERS infections during pregnancy)
- Vertical transmission of COVID-19: no (limited data)

- **Children With HIV**
- Limited data indicates children appear less likely to become severely ill with COVID-19 than older adults
- Subpopulations of children may be at increased risk of more severe COVID-19
  - Non-COVID-19 coronaviruses: younger age, underlying pulmonary pathology, and immunocompromising conditions were associated with more severe outcomes
- All immunizations should be up to date (including influenza and pneumococcal vaccines)

- Department of Health and Human Services. Interim guidance for COVID-19 and persons with HIV. June 19, 2020. https://clinicalinfo.hiv.gov/en/guidelines/

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DHHS: Guidance for Persons With HIV

In Self-Isolation or Quarantine Due to SARS-CoV-2 Exposure

- Healthcare workers should
  - Verify that patients have adequate supplies of all medications and expedite additional drug refills as needed
  - Devise a plan to evaluate patients if they develop COVID-19-related symptoms, including for possible transfer to a healthcare facility for COVID-19-related care
- Persons with HIV should
  - Contact their healthcare provider to report that they are self-isolating or in quarantine
  - Inform their healthcare provider how much ARV medications and other essential medications they have on hand

With Fever or Respiratory Symptoms and Are Seeking Evaluation and Care

- Healthcare workers should
  - Follow CDC recommendations, as well as state and local health department guidance on infection control, triage, diagnosis, and management
- Persons with HIV should
  - Follow CDC recommendations regarding symptoms
  - Call clinic in advance before presenting to care providers
  - Use respiratory/hand hygiene/cough etiquette (face mask)
  - If they present to a clinic or an emergency facility without calling in advance, alert staff of symptoms

- Department of Health and Human Services. Interim guidance for COVID-19 and persons with HIV. June 19, 2020. https://clinicalinfo.hiv.gov/en/guidelines/

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DHHS: Guidance for Managing Persons With HIV Who Develop COVID-19

- **Hospitalization Is not Necessary**
- Persons with HIV should
  - Manage symptoms at home with supportive care for symptomatic relief
  - Maintain close communication with their healthcare provider and report if symptoms progress (eg, sustained fever for >2 days, new shortness of breath)
  - Continue their ARV therapy and other medications, as prescribed

- **Hospitalized**

Persons with HIV should

- Continue ART
  - If on ibalizumab IV q2 weeks: arrange with hospital provider to continue without interruption
  - If on investigational ARV medication: arrange with investigational study team to continue if possible
- Avoid ARV drug substitutions
  - If substitution is necessary, refer to DHHS guidelines on ARV drugs that can be switched for persons with HIV in disaster areas
- Critically ill patients who require tube feeding, some ARV medications are available in liquid formulations and some, but not all, pills may be crushed

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DHHS: Guidance for Managing PWH With COVID-19

- Investigational/marketed drugs being evaluated may be available via compassionate use or off-label use

- For patients receiving COVID-19 treatment
  - Assess DDI potential with ART

- When available, clinicians may consider enrolling patients in a clinical trial evaluating the safety and efficacy of experimental treatment for COVID-19
  - Persons with HIV should not be excluded from these trials
  - Clinicaltrials.gov is a useful resource to find studies investigating potential treatments for COVID-19

- DHHS. June 19, 2020. https://clinicalinfo.hiv.gov/en/guidelines/covid-19-and-persons-hiv-interim-guidance

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Phase 3 COVID-19 Vaccine Trials That Include PWH

	Mechanism	Sponsor	ClinicalTrials.gov Identifier
AZD1222	Replication deficient viral vector vaccine (adenovirus from chimpanzees)	University of Oxford, AstraZeneca	NCT04516746
CoronaVac	Inactivated vaccine (formalin with alum adjuvant)	Sinovac	NCT04582344
JNJ-78436735	Non-replicating viral vector	Johnson & Johnson	NCT04505722
mRNA-1273	mRNA-based vaccine	Moderna	NCT04470427
NVX-CoV2373	Nanoparticle vaccine	Novavax	Conducted in UK (EudraCT 2020-004123-16)
Bacillus-Calmette-Guerin vaccine	Live attenuated vaccine	University of Melbourne and Murdoch Children's Research Institute, Radboud University Medical Center, Faustman Lab at Massachusetts General Hospital	NCT04414267 NCT04534803 NCT04327206
BNT162b2	mRNA-based vaccine	Pfizer, BioNTech	NCT04368728

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Ending the HIV Epidemic: A Plan for America

GOAL:

75% reduction in new HIV infections in 5 years and at least **90%** reduction in 10 years.

HHS will work with each community to establish local teams on the ground to tailor and implement strategies to:

- **Diagnose** all people with HIV as early as possible.
- **Treat** the infection rapidly and effectively to achieve sustained viral suppression.
- **Prevent** new HIV transmissions by using proven interventions, including pre-exposure prophylaxis (PrEP) and syringe services programs (SSPs).
- **Respond** quickly to potential HIV outbreaks to get needed prevention and treatment services to people who need them.

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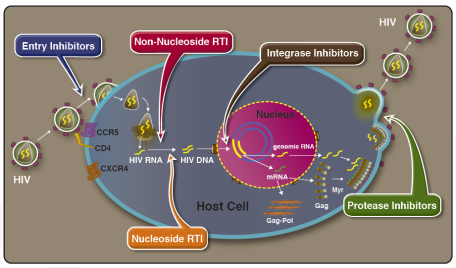
Update – HIV Treatment

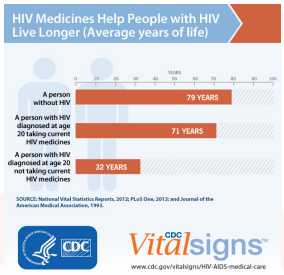
Antiretroviral Mechanism of Action



http://depts.washington.edu/nwaetc/Pill_Chart.pdf

Treatment Goals

- Maximally and durably suppress plasma HIV RNA
- Restore and preserve immunologic function
- Reduce HIV-associated morbidity and prolong the duration and quality of survival
- Prevent HIV transmission *"Treatment as Prevention"*



https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/9/treatment-goals

Considerations When Starting Antiretroviral Therapy

- Who to start on antiretroviral therapy-
  - Now DHHS, WHO and IAS-USA all recommend starting ART in everyone diagnosed with HIV irrespective of their CD4 count
- When to start antiretroviral therapy –
  - Now DHHS, WHO and IAS-USA all recommend starting ART as soon as possible
  - Rapid start or initiating ART on same day as HIV is diagnosed is an emerging strategy to reduce loss to follow-up and decrease time to viral suppression
- What antiretroviral to start
- When to switch antiretroviral therapy
- What to switch to

What Antiretroviral Therapy to Start –Considerations:

- Viral load and CD4 count
- HIV resistance test result
- Drug interactions
- Potential side effects
- Pill burden
- Access and Cost

Recommended Initial Regimens for Most People With HIV

Class	DHHS[1]	IAS-USA[2]
INSTI	▪ BIC/FTC/TAF* ▪ DTG/ABC/3TC* ▪ DTG + (FTC or 3TC)/(TAF or TDF) ▪ RAL + (FTC or 3TC)/(TAF or TDF) ▪ DTG/3TC**	▪ BIC/FTC/TAF* ▪ DTG + FTC/TAF, TDF/FTC or 3TC ▪ DTG/3TC***

***Single tablet regimens**
**** (if HIV VL < 500,000, no hepatitis B infection and genotype shows no resistance – do not use for rapid start prior to testing results)**
***** not for rapid start and CD4 <200**

Example of Studies of Recommended INSTIs as First-Line ART Regimens

Trial	INSTI Regimen	Comparator	Wks	Results	Outcome vs Comparator
GS-1489[1]	**BIC**/FTC/TAF	DTG/ABC/3TC	96	88 vs 90%	Noninferior
GS-1490[2]	**BIC**/FTC/TAF	DTG + FTC/TAF	96	84 vs 86%	Noninferior
SINGLE[3]	**DTG** + ABC/3TC	EFV/FTC/TDF	144	71 vs 63%	Favors INSTI
FLAMINGO[4]	**DTG** + 2 NRTIs	DRV + RTV + 2 NRTIs	96	80 vs 68%	Favors INSTI
SPRING-2[5]	**DTG** + 2 NRTIs	RAL + 2 NRTIs	96	81 vs 76%	Noninferior
GEMINI[6]	DTG + 3TC	DTG plus TDF/FTC	96	86 vs 89.5%	Noninferior

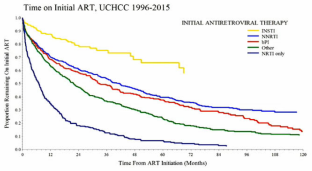
- No resistance mutations (INSTI or NRTI) in treatment naïve studies of dolutegravir or bictegravir
- Rates of discontinuation for AEs numerically lower with INSTIs vs PIs or NNRTIs
- Modest difference in adverse events between arms in head-to-head comparisons of dolutegravir with bictegravir if dolutegravir given with abacavir

1. DA Wohl et al. Lancet HIV 6 (6), e355-e363. Jun 2019. 2. HJ Stellbrink et al. Lancet HIV 6 (6), e364-e372. Jun 2019. 3. Walmsley. JAIDS. 2015;70:515. 4. Molina. Lancet HIV. 2015;2:e127. 5. Raffi. Lancet Infect Dis. 2013;13:927. 6. Cahn. IAS 2019. Abstr WEAB0404LB.

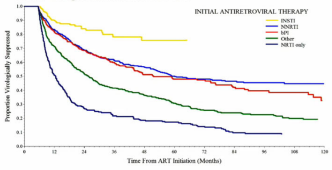
Increased Persistence Of Initial Art With INSTI-containing Regimens

Thibaut Davy, Sonia Napravnik, Oksana Zakharova, Joseph J. Eron

Time on Initial ART, UCHCC 1996-2015



Time to Virologic Failure, UCHCC 1996-2015



	Discontinuation HR (95% CI)	Virologic failure HR (95% CI)
INSTI	0.49 (0.35, 0.69)	0.70 (0.46, 1.06)
bPI	1.24 (1.05, 1.47)	1.24 (1.01, 1.53)
Other	1.47 (1.24, 1.75)	1.21 (0.99, 1.46)
NRTI	2.98 (2.38, 3.74)	1.72 (1.35, 2.19)
NNRTI	Ref.	Ref.

Davy-Mendez T, Eron JJ, Zakharova O, Wohl DA, **Napravnik S.** J Acquir Immune Defic Syndr. 2017 Oct 1;76(2):111-115.

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Low Virologic Failure and Treatment Emergent Resistance with Dolutegravir and Bictegravir

Trial Name	Follow-up, Wks	Treatment Arm	Virologic Failure, n (%)	Treatment-Emergent Primary Mutations, n
SPRING-2[1]	96	DTG + 2 NRTI (n = 411)	22 (5)	0
		RAL + 2 NRTIs (n = 411)	29 (7)	1 (INSTI), 4 (NRTI)
SINGLE[2]	144	DTG + ABC/3TC (n = 414)	39 (9)	0
		EFV/TDF/FTC (n = 419)	33 (8)	1 (NRTI),6 (NNRTI)
FLAMINGO[3]	96	DTG + 2 NRTI (n = 242)	2 (< 1)	0
		DRV/R + 2 NRTI(n = 242)	4 (2)	0
GS-1489[4]	96	BIC/F/TAF (n =316)	3 (1)	0
		DTG/ABC/3TC (n= 315)	8 (2.5)	0
GS-1490[5]	96	BIC/F/TAF (n =320)	14 (4)	0
		DTG + TAF/FTC (325)	4 (1)	0
Gemini 1 and 2[6]	144	DTG/3TC (n= 716)	6	0
		DTG + TDF/FTC (n = 717)	4	1

Raffi F, et al. *Lancet Infect Dis.* 2013;13:927-935. 2. Pappa K, et al. ICAAC 2014. Abstract H-647a. 3. Molina JM, et al. Glasgow HIV 2014. Abstract O153. DA Wohl et al. Lancet HIV 6 (6), e355-e363. Jun 2019. 5. HJ Stellbrink et al. Lancet HIV 6 (6), e364-e372. Jun 2019. 6. Cahn. IAS 2019. Abstr

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Integrase Inhibitors Considerations

- There maybe transmitted resistance with integrase resistance but very rare
- Women of childbearing potential – risk of birth defects continues to fall
- Possible weight gain – now convincingly associated with weight gain
- Will there be impact of generics on cost ?

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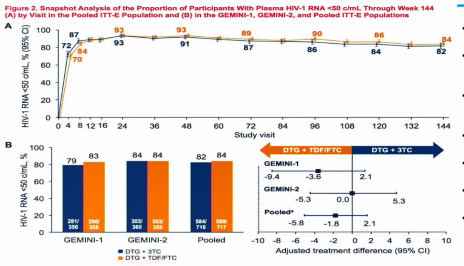
Dual therapy

- GEMINI-1,-2 and TANGO: Virologic Outcomes With DTG + 3TC as Initial or Switch Therapy
- **GEMINI-1,-2:** Initial therapy with DTG + 3TC noninferior to DTG + TDF/FTC for primary endpoint of HIV-1 RNA < 50 c/mL
- **TANGO:** Switch to DTG/3TC noninferior to continued TAF-based ART for primary endpoint of HIV-1 RNA ≥ 50 c/mL

Gemini-1 and -2: 144 week data



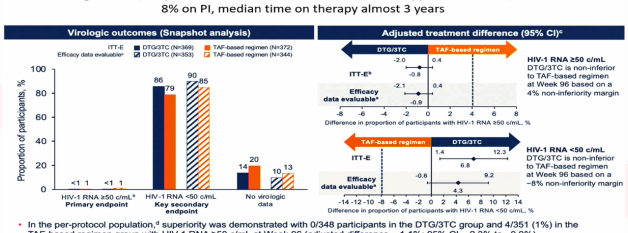
- 716 and 717 participants per arm 2- vs. 3- drugs
- Only 23 and 21 participants with HIV RNA ≥ 50 at week 144 or at discontinuation
- 109 and 97 participants missing data or discontinued while suppressed
- Fewer drug-related AE 20% vs. 27% with 2 drugs
- Weight change: 3.7 vs. 2.4 kg 2 vs. 3-drug therapy
- Renal and bone markers favor 2-drug therapy
- Withdrawal – renal related 2 vs. 12 participants

Dolutegravir Plus Lamivudine Versus Dolutegravir Plus Tenofovir Disoproxil Fumarate and Emtricitabine in Antiretroviral-Naive Adults With HIV-1 Infection (GEMINI-1 and GEMINI-2): Week 48 Results From Two Multicentre, Double-Blind, Randomised, Non-Inferiority, Phase 3 Trials , Lancet 2019 Jan

Tango

TANGO 96 week Data: Switch TAF-based to DTG/3TC

No h/o virologic failure, no previous INSTI or NRTI resistance or HBV, approx. 79% INSTI, 13% NNRI and 8% on PI, median time on therapy almost 3 years



- In the per-protocol population,[d] superiority was demonstrated with 0/348 participants in the DTG/3TC group and 4/351 (1%) in the TAF-based regimen group with HIV-1 RNA ≥50 c/mL at Week 96 (adjusted difference, −1.1%; 95% CI, −2.3% to −0.0%)

*Sensitivity analysis excluding 16 and 20 participants in the DTG/3TC and TAF-based regimen groups, respectively, because of no Week 96 HIV-1 RNA data due to effects of the COVID-19 pandemic. †Primary endpoint (Snapshot virologic non-response, ITT-E). ‡Based on Cochran-Mantel-Haenszel stratified analysis [DTG/3TC − TAF-based regimen] adjusting for baseline third agent class. §Sensitivity analysis.

Van Wyk et al Glasgow2020

How Commonly Will 2 drugs Be Used

- Multiple unboosted combinations approved or in development (DTG/3TC. DTG/ RPV and cabotegravir/RPV)
- Few differences yet in AE or long term outcomes
- No substantial cost differences
- Fewer metabolic effects – no TAF?

Effect of Switching ART on Weight and Metabolic Changes

Study	Switch	Weight/Metabolic Changes
OPERA (observational) Mallon AIDS 2020, OAB0604	TDF to TAF	2-4.5 kg/yr; greatest in those also switching to newer INSTI (DTG, BIC)
TRIO (observational) McComsey, IDWeek, 2020, LB7	TDF or ABC to TAF	Greater weight gain after switching from TDF to TAF than after switching from ABC to TAF
TANGO (randomized) van Wyk AIDS 2020 #0606	TAF-based regimen to DTG/3TC	Weight: no difference DTG/3TC: Improved lipids, insulin resistance, especially after switching from boosted regimen

OPMAN 2020

When to switch antiretroviral therapy ?

- Adverse events,
- Drug-drug or drug-food interactions
- Pill burden, cost, simplification
- Virologic failure

Long acting antiretrovirals – cabotegravir

- Integrase inhibitor similar to dolutegravir
- Similar resistance profile
- Initially will require an oral lead in
- Injected into Gluteus Medius
- Exciting -Nanotechnology formulation : SC and IM injections
- Safety- mostly injection site reactions and nodules with SC dosing
- Pase1,2 and 3 completed
- RPV long acting needs cold chain

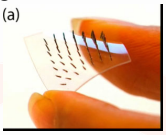
Cabotegravir: Phase 3 trials

Study (reference)	Study population	Design	Result (week 48)
FLAIR Orkin NEJM 2020;382:1124-1135	Rx-naïve adults (N=629)	ABC/3TC/DTG X 20 wks → CAB + RPV (oral X 4 wks, then IM monthly) or continue oral regimen (non-inferiority Δ6%)	VS >93%; CAB + RPV **non-inferior** to oral regimen Glasgow 2020: 144 wks
ATLAS Swindells NEJM 2020;382:1112-1123	Adults with VS on 2 NRTI + PI, NNRTI, or INSTI (N=616)	continue ART or change to CAB + RPV (oral X 4 weeks, then IM monthly) (non-inferiority Δ6%)	VS >92%; CAB + RPV **non-inferior** to oral regimen Glasgow 2020: 96 wks
ATLAS-2M Overton CROI 2020 Abstract 34	Adults on SOC ART or CAB + RPV LA with VL <50 (N=1045)	CAB 400 + RPV 600 LA IM q4 wks or CAB 600 + RPV 600 LA IM q8 wks (non-inferiority Δ4%)	VS >93%; CAB + RPV q8 wks **non-inferior** to q4 wks

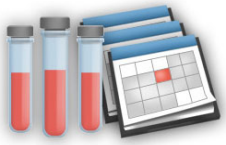
Drugs in the Pipeline

- CAB – Prodrug in Rhesus Macaques – Nano formulated
- Has extended release Q6 month dosing
- Cabotegravir – Micro needle Patches

(a)



Pre-exposure Prophylaxis



PrEP IS AN HIV PREVENTION METHOD IN WHICH PEOPLE WHO DO NOT HAVE HIV INFECTION TAKE A PILL DAILY TO REDUCE THEIR RISK OF BECOMING INFECTED

ONLY PEOPLE WHO ARE HIV-NEGATIVE SHOULD USE PrEP. A NEGATIVE HIV TEST IS REQUIRED BEFORE STARTING PrEP AND THEN EVERY 3 MONTHS WHILE TAKING PrEP.

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http://aids.gov/hiv-aids-basics/prevention/reduce-your-risk/pre-exposure-prophylaxis

Why PrEP?

- Estimated 50,000 new HIV infections each year in the US
  - No cure
  - No effective vaccine yet
- In multiple studies, there is a significantly decreased risk of HIV acquisition in those who took PrEP consistently

Transmission Route	Effectiveness Estimate	Interpretation
Sexual	~99%	Very high levels of adherence to PrEP ensures maximum effectiveness.
Injection drug use	74% – 84%	These estimates are based on tenofovir alone and not necessarily when taken daily. The effectiveness may be greater for the two-drug oral therapy and if used daily.

CDC.gov. PrEP FAQs. Available at https://www.cdc.gov/hiv/clinicians/prevention/prep.html. Accessed 12.15.2019.

ESTIMATED NUMBER OF ADULTS WHO COULD POTENTIALLY BENEFIT FROM PREP, UNITED STATES, 2015

	Gay, bisexual, or other men who have sex with men	Heterosexually active adults	Persons who inject drugs	Total by race/ethnicity
Black/African American, non-Hispanic	309,190	164,660	26,490	500,340
Hispanic/Latino	220,760	46,580	14,920	282,260
White, non-Hispanic	238,670	36,540	28,020	303,230
Total who could potentially benefit from PrEP	**813,970**	**258,080**	**72,510**	**1,144,550**

Notes: PrEP=pre-exposure prophylaxis; data for "other race/ethnicity" are not shown

CDC U.S. Department of Health and Human Services Centers for Disease Control and Prevention

Smith, DK., et al. CROI 2018; March 4-7, Boston, MA, USA.

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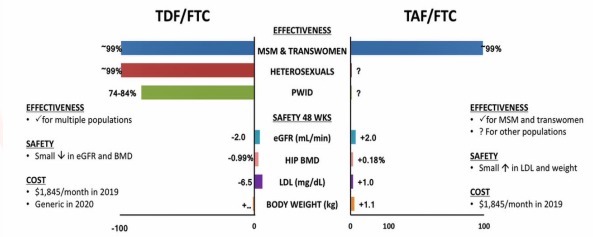
2 FDA-Approved Medications for PrEP

Each consists of two drugs combined in a single oral tablet taken daily

1. Emtricitabine (F) 200 mg combined with tenofovir disoproxil fumarate (TDF) 300 mg (F/TDF – brand name **Truvada**®)
2. Emtricitabine (F) 200 mg combined with tenofovir alafenamide (TAF) 25 mg (F/TAF – brand name **Descovy**®)

Approved to prevent HIV infection in adults and adolescents weighing at least 77 pounds (35 kg)

Which medication should I prescribe for daily PrEP



Fda.gov.media/129607/download-cdc.gov/hiv/risk/estimates/prevention strategies.html

Table 1: Summary of Guidance for PrEP Use

	Men Who Have Sex with Men	Heterosexual Women and Men	Persons Who Inject Drugs
Detecting substantial risk of acquiring HIV infection	HIV-positive sexual partner Recent bacterial STI† High number of sex partners History of inconsistent or no condom use Commercial sex work	HIV-positive sexual partner Recent bacterial STI‡ High number of sex partners History of inconsistent or no condom use Commercial sex work In high HIV prevalence area or network	HIV-positive injecting partner Sharing injection equipment
Clinically eligible	Documented negative HIV test result before prescribing PrEP No signs/symptoms of acute HIV infection Normal renal function; no contraindicated medications Documented hepatitis B virus infection and vaccination status		
Prescription	Daily, continuing, oral doses of TDF/FTC (Truvada), ≤90-day supply		
Other services	Follow-up visits at least every 3 months to provide the following: HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment At 3 months and every 6 months thereafter, assess renal function Every 3-6 months, test for bacterial STIs		
	Do oral/rectal STI testing	For women, assess pregnancy intent Pregnancy test every 3 months	Access to clean needles/syringes and drug treatment services

STI: sexually transmitted infection

Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2017 Update Clinical Practice Guideline

Ready, Set, PrEP

- Launched by the US Department of Health and Human Services on 12/3/19
- To qualify, patients must:
  -test negative for HIV
  -have a valid prescription from a healthcare provider
  -not have prescription drug coverage
- Beginning no later than March 30, 2020, patients may obtain PrEP through CVS, Walgreens, Rite Aid or mail order all at no cost
- https://www.getyourprep.com/ or 855-447-8410
- HIV.gov Locator

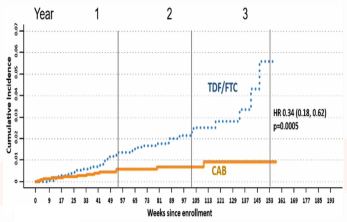
HPTN 083- PrEP with IM CAB vs TDF/FTC

- Phase 3 randomized double blinded HIV PrEP international study
- Study population : High risk adult MSM/TGW (n=4750)
- Study population 67% 30 years
- 12 % TGW
- Cabotegravir oral lead in 5 weeks ->IM q2 months vs TDF/FTC po daily

HPTN 083- PrEP with IM CAB vs TDF/FTC

- Results :
- DSMB stopped study early
- New HIV infections 13 (CAB) vs 39(TDF/FTC)
- HIV incidence 0.41(CAB) vs 1.22(TDF/FTC)

Conclusion CAB non inferior and superior



Original Investigation

Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy

Alison J. Rodger, MD; Valentina Cambiano, PhD; Tina Bruun, RN; Pietro Vernazza, MD; Simon Collins; Jan van Lunzen, PhD; Giulio Maria Corbelli; Vicente Estrada, MD; Anna Maria Geretti, MD; Apostolos Beloukas, PhD; David Asboe, FRCP; Pompeyo Viciana, MD; Félix Gutiérrez, MD; Bonaventura Clotet, PhD; Christian Pradier, MD; Jan Gerstoft, MD; Rainer Weber, MD; Katarina Westling, MD; Gilles Wandeler, MD; Jan M. Prins, PhD; Armin Rieger, MD; Marcel Stoeckle, MD; Tim Kümmerle, PhD; Teresa Bini, MD; Adriana Ammassari, MD; Richard Gilson, MD; Ivanka Krznaric, PhD; Matti Ristola, PhD; Robert Zangerle, MD; Pia Handberg, RN; Antonio Antela, PhD; Sris Allan, FRCP; Andrew N. Phillips, PhD; Jens Lundgren, MD; for the PARTNER Study Group

- The PARTNER1 study looked at 888 couples where one was HIV positive and on antiretroviral treatment (ART) and who were already having sex without condoms:

-548 heterosexual couples

-340 MSM

- They found that in more than 58,000 acts of condomless sex there were no HIV transmissions from the HIV positive partner among those on treatment with an undetectable viral load
- Couples were followed for a median of 1.3 years

JAMA. 2016;316(2):171-181. doi:10.1001/jama.2016.5148

Partner2 Study:

- Prospective observational study in 14 European countries
- Enrolled 927 homosexual serodiscordant couples between September 2010 and July 2017
- Positive partner was on suppressive ART
- A total of 74568 condomless-sex acts were reported, with 0 cases of within couple HIV transmission

http://programme.aids2018.org/Abstract/Abstract/13470

QUESTIONS?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THANK YOU!